

REMARKS

No claim has been added or canceled in this response. Claim 3 has been amended to correct typographical errors. Claim 9 has been amended to properly depend from claim 1. No new matter has been added. With entry of the amendment, claims 1, 3-9 and 21 will be pending in the application.

Claim objection

Claim 9 has been objected to as being of improper dependent form. The Examiner states that the term "water-insoluble material" lacks antecedent basis in claim 1. Claim 9 has been amended to recite a hydrophobic material rather than a water-insoluble material. Reconsideration and withdrawal of the objection are respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1, 3, 5-9 and 21 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over U.S. Patent No. 4,371,516 to Gregory *et al.* ("Gregory") in view of U.S. Patent No. 4,721,709 to Seth *et al.* ("Seth"). The Examiner states that "Gregory et al. discloses shaped articles having a porous open matrix network of water-soluble or water-dispersible carrier (col. 2, lines 37-40), the articles carrying a chemical (as to instant claim 7), the article being capable of being rapidly disintegrated by water (col. 1, lines 58-64), wherein the article comprise: A) a polysaccharide, polyvinyl alcohol, polyvinyl pyrrolidone or mixtures thereof; B) a surfactant, such as polyoxyethylene sorbitan monooleate (col. 4, lines 5-8)." The Examiner also states that "The shaped articles are produced by freeze drying of a composition (col. 3, lines 63-65). The shaped articles comprise cylindrical or other shapes." January 14, 2010 Office Action at page 9. The Examiner appears to concede that Gregory does not teach porous bodies having an oil-in-water emulsion-formed lattice, but alleges that it would have been "obvious to a skilled artisan that depending on the specific drug, i.e. hydrophilic or hydrophobic, a specific co-solvent appropriate for increasing solubility of that drug, should be used." Office Action at page 4. The Examiner further states that "(s)ince Gregory et al discloses the porous moulded articles produced by freeze-drying the composition comprising a chemical and a carrier material including a water solvent and a co-solvent (which in the case of the hydrophobic drug will be an oily phase), therefore, it would have been obvious to a skilled artisan that freeze-drying of the composition will produce pores from both water phase and an oil phase as well." *Id.*

Applicants respectfully traverse and submit that a *prima facie* case of obviousness has not been established.

Gregory discloses a pharmaceutical (or other chemical) dosage form that is rapidly disintegrable. This is achieved by providing a "shaped" article comprising an open matrix network of water-soluble or water-dispersible polymeric carrier material carrying a chemical (see, for example, col. 1, lines 21-24, 34-36, 44-49, 54-57 and 58-64). It is said that the open matrix network is similar in structure to a solid foam (col. 2, lines 48-49) and that rapid disintegration of said matrix results in the rapid release of any pharmaceutical or other chemical carried by the matrix (col. 2, lines 58-60). The dosage form is prepared by freeze-drying a composition comprising the pharmaceutical and a solution of the carrier material in solvent, and optionally other ingredients such as a surfactant (col. 3, line 57 to col. 4, line 7).

Applicants respectfully disagree with the Examiner's statement that one of skill in the art, when viewing Gregory, would have been motivated to include a co-solvent that would lead to formation of an emulsion when mixed with the aqueous solution of the polymeric carrier material. While Gregory does mention the possible use of a co-solvent, it is stated that that "(t)he solvent is preferably water but it may contain a co-solvent (such as an alcohol e.g. tert-butyl alcohol) to improve the solubility of the chemical" (col. 3, line 68 to col. 4, line 2). The only co-solvents mentioned are water-miscible alcohols, which would not form an emulsion when added to the aqueous polymer solution.

If one of skill in the art were to turn to the Examples in Gregory for further guidance, one would find that in Example 1, part (a) concerns formation of a hydrolysed gelatin solution by dissolving gelatin in water, while part (b) concerns preparation of the pharmaceutical dosage form by **mixing** lorazepam (the pharmaceutical), a colouring agent and a flavouring agent with the gelatin solution. With continued mixing, the mixture is injected into depressions into a liquid nitrogen-cooled stainless steel tray. The trays are then subjected to freeze-drying which results in a number of moulded bodies containing lorazepam. Importantly, nowhere in Example 1 is the lorazepam dissolved, or an emulsion formed with the gelatin solution.

Examples 2 through 11 of Gregory are similar to Example 1, but use other pharmaceutical agents and optional other components. Specifically, the Examples use the following:

Example 2: nitroglycerin

Example 3: digoxin

Example 4: ergotamine

Example 5: lorazepam plus Tween 80 and sucrose

Example 6: meptazinol and sucrose

Example 7: oxaprozin and sucrose, "the oxaprozin being **dispersed** in the gelatin solution with the aid of ultrasonic vibrations" (col. 5, lines 44-45, emphasis added)

Example 8: lorazepam plus sodium alginate, dextran, dextrose and distilled water, "the lorazepam being **suspended** in the water containing sodium alginate, dextran and dextrose with the aid of ultrasonic vibrations" (col. column 5, lines 53-56, emphasis added)

Example 9: lorazepam plus dextrin, polyvinylpyrrolidone, Tween 80 and distilled water

Example 10: lorazepam plus polyvinylalcohol, polyvinylpyrrolidone, sucrose, Tween 80 and distilled water, in which "the lorazepam is added and **dispersed** with the aid of ultrasonic vibrations" (col. 6, lines 9-11, emphasis added)

Example 11: lorazepam plus acacia, sucrose, polyvinylpyrrolidone, Tween 80 and distilled water, in which "the lorazepam (**is**) **dispersed** into the solution with the aid of ultrasonic vibrations" (col. 6, lines 27-28, emphasis added).

As is evident above, when considering Gregory as a whole, one does not find a teaching or suggestion of porous bodies having an oil-in-water emulsion-formed lattice. Rather, Gregory teaches either dissolving the active agent in water or a water-miscible solvent, or dispersion or suspension of an active agent in an aqueous solution. Accordingly, Gregory does not teach or suggest an oil-in-water emulsion-formed lattice, nor a porous body having pores that are "from the sublimation of the oil phase of the emulsion" as required by claim 1.

The Examiner states that the element "oil-in-water emulsion-formed" is a product by process limitation. Office Action at page 5. Applicants respectfully disagree and submit that this form should be considered in defining the porous bodies of claim 1 as emulsion-formed, as the structure that results from an oil-in-water emulsion differs from other structures such as those resulting from other structures such as those resulting from a water-in-oil emulsion. MPEP 2113 states that "(t)he structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garner*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)."

"Emulsion-templating" is a term of art, which distinguishes the porous bodies of claim 1 from other generic porous bodies, of which there are many. Attached as Exhibit A are excerpts from a book, *Porous Materials – Process Technology and Applications* by Kozo Ishizaki, Sridhar Komamneni and Makoto Nanko. At page 5, under the heading *Classification of Porous Materials*, this reference teaches that there are many different types of porous materials, for use

in many different applications, which are classified by a number of criteria including pore size, pore shape, materials and **production methods**. Page 8 provides a table (Table 1.2) which summarizes the different classes of porous materials (a-g) and their respective production methods. Emulsion-templated bodies are a sub-set of foamed porous bodies. Further information regarding the theory behind emulsion-templating can be found in Exhibit B, from the following web page:

<http://www.liv.ac.uk/chemistry/res/coopergroup/research/emulstemplate.html>

Accordingly, this term of art should be considered in defining the porous bodies of claim 1 as being emulsion-formed, and therefore distinguishable from other porous bodies.

The Examiner cites Seth in the rejection, but only mentions it as disclosing that "clonazepam is a hydrophobic drug which is known to be adsorbed onto a carrier to form adsorbate, followed by freeze-drying (see col. 7, lines 48-55; col. 13, lines 45-65 of Seth et al)." Office Action at page 4. Applicants submit that Seth does not disclose an emulsion-formed lattice, and therefore does not remedy the deficiencies of Gregory described above.

Seth discloses providing a "dry powder pharmaceutical composition containing a hydrophobic, poorly soluble drug that is adsorbed onto a pharmaceutical carrier." Seth at col. 4, lines 44-47. The process for making such a composition comprises "mixing (1) a solution comprising said hydrophobic drug in a solvent for said drug (2) a suspension comprising said carrier suspended in said solvent for the drug and (3) a non-solvent for the said drug which is miscible with the said solvent for the drug said mixing being effected under suitable conditions such as for example by rapid agitation causing the precipitation of said drug having the particle-size characteristics set out above and finally (4) drying the resulting drug-carrier mixture to a dry powder form." *Id.* at col. 4, lines 56-68. See also col. 6, lines 40-52.

In Example 1, oxazepam (the drug) is dissolved in ethanol to form a solution; corn starch (the carrier material) is added to the solution and stirred until a uniform suspension is obtained. This suspension is then decanted into water with continuous rapid stirring until a milky white suspension is obtained. The ethanol is then removed from the suspension to leave an aqueous suspension, which is then spray-dried to leave particles of corn starch on which the oxazepam is adsorbed.

Examples 2 and 3 repeat the process of Example 1, but substitute acetone for ethanol and microcrystalline cellulose or montmorillonite for corn starch respectively.

Examples 4, 5 and 6 use the product made in Examples 1, 2 and/or 3.

Example 7 is similar to Example 1 in that temazepam (the drug) is dissolved in ethanol to form a solution; corn starch (the carrier material) is added to the solution and stirred until a

uniform suspension is obtained. This suspension is then poured slowly into water with continuous rapid stirring until a final suspension is obtained, which is then spray-dried to leave particles of corn starch on which the temazepam is adsorbed.

In summary, Seth teaches dissolving a drug in a solvent but teaches that the carrier material is subsequently added and dispersed in this solution to form a suspension, which is subsequently spray-dried to form particles of the carrier material on which the drug is adsorbed. There is no disclosure of porous bodies having an oil-in-water emulsion-formed lattice in Seth.

In view of the foregoing, Gregory or Seth, taken alone or in combination, do not teach or suggest the subject matter of claim 1. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1, 3, 5-9 and 21 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Gregory in view of U.S. Patent No. 5,660,857 to Haynes *et al.* ("Haynes"). The Examiner states that "(t)ough Gregory et al does not explicitly state the lattice being formed from oil-in-water emulsion and specify the porous bodies having two types of pores as recited in instant claim 1, however, Haynes et al further discloses a process for preparing a composite comprising preparing an oil-in-water-emulsion followed by freeze drying the emulsion (col. 2, lines 40-42) to form a sponge (col. 2, lines 30-31). The oil phase is used for dissolving oestradiol hydrophobic drug (col. 4, lines 34-36; col. 2, lines 50-51)." Office Action at page 6.

Applicants respectfully traverse and submit that a *prima facie* case of obviousness has not been established.

Gregory has been discussed above. Haynes discloses a process for preparing a composite comprising an insoluble protein matrix and an oleaginous material (i.e. an oily material) which is useful as a material for, e.g., surgical dressings (on account of its water-insolubility). See, for example, col. 1, lines 11-16. The composite is prepared by mixing a protein, the oleaginous material and water to form an emulsion of the oleaginous material in an aqueous dispersion of the protein, and subsequently drying the emulsion to remove the water only. The final product still contains the oleaginous material and is therefore actually a dry emulsion. Specifically, Haynes states that "a biopolymer matrix based on an insoluble protein can be formed with **significant quantities of an oleaginous material held within the matrix itself** (rather than physically entrapped within the pores of such a matrix), and that such a material exhibits a surprisingly non-oily or non-greasy appearance and feel." Haynes at col. 1, line 66 to col. 2, line 5 (emphasis added). Haynes also states that "the emulsion is frozen and then freeze dried, to form a sponge, the matrix of the sponge being formed of the insoluble

protein/oleaginous material composite. In this embodiment, too, the oleaginous material may appear as discrete microscopic droplets when surface of the sponge matrix is viewed." *Id.* at col. 2, lines 30-35. Finally, the Examples refer to a collagen/oil sponge, collagen/oil film, or collagen/oil microspheres. The formation of a dry emulsion, which when added to water would reform the original emulsion due to the continued presence of the oil, is quite different from the emulsion-formed porous bodies of claim 1 which would not reform the original emulsion upon addition to water. Additionally, as the oil remains present in the final product, the composite would not have pores formed "from the sublimation of the oil phase of the emulsion" as required by claim 1.

In sum, Haynes does not disclose creating porous bodies that are water soluble, such that hydrophobic materials that are contained in the emulsion-formed lattice are dispersed when the porous bodies are exposed to an aqueous medium. Accordingly, one of skill in the art would not have been motivated to combine Haynes with Gregory, and even if one of skill in the art were to combine the references, one would not arrive at the subject matter of claim 1.

Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1, 3-9 and 21 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Gregory in view Haynes, in further view of U.S. Patent No. 5,648,093 to Goye *et al.* ("Goye"), U.S. Patent No. 5,502,082 to Unger *et al.* ("Unger"), and Japanese Patent Application No. JP 01011141 to Fujimoto *et al.* ("Fujimoto").

Applicants respectfully submit that as discussed above, one of skill in the art, when viewing Gregory or Haynes alone or in combination, would not have been motivated to produce the subject matter of the pending claims. None of Goye, Unger and Fujimoto remedy the deficiencies of Gregory or Haynes. Applicants therefore need not, and do not, address the Examiner's contentions with regard to Goye, Unger and Fujimoto, and certain aspects of claims 1, 3-9 and 21. By not addressing those contentions, Applicants in no way acquiesce to them. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 3-9 and 21 depend either directly or ultimately from claim 1, and accordingly are allowable for at least the reasons set forth above and may be further patentable for additional reasons. Reconsideration and withdrawal of the rejections are respectfully requested.

CONCLUSION

In view of the foregoing, Applicants submit that the claims are in condition for allowance. Favorable consideration of the present application is therefore respectfully requested. If a conference call would be useful in resolving issues arising from the filing of this communication, please contact the undersigned at the below-noted number.

Respectfully submitted,

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